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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,602	05/03/2002	Dan L. Eaton	P3230R1C001-168	4335

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,602	EATON ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6/24/05.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-5 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 03 May 2002 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7/27/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, and/or Claims

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid.

The Response and Amendments, submitted 24 June 2005, have been entered. The Information Disclosure Statement, submitted 27 July 2005, has been entered. Claim 1 is amended. Claim 6 is canceled.

Claims 1-5 are under examination in the Instant Application.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

Continuity

The objection to the Specification for not complying with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119, is *withdrawn,* based on Applicant's arguments (page 3, 24 June 2005). The filing date of the PCT Application (24 August 2000) is considered as the priority date.

Maintained/New Objections and/or Rejections

35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.

Claims 1-5 are rejected under 35 U.S.C. 101, as lacking utility. The reasons for this rejection under *35 U.S.C. § 101* are set forth at pages 4-10 of the previous Office Action (23 December 2004). Claims 1-5 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (23 December 2004), one skilled in the art clearly would not know how to use the claimed invention.

Applicants argue (*Remarks*, 24 June 2005, page 3 and throughout) that the data presented in the instant Specification are enabling for the cognate antibody of the polypeptide of SEQ ID NO: 94. They argue that the PRO1328 nucleic acid is a diagnostic marker for normal lung tissue and melanoma tumor and point to the results of the expression assay (pages 3 and 8, 24 June 2005).

Applicant's arguments (24 June 2005) have been fully considered but are not found to be persuasive for the following reasons:

In the instant case, the specification provides data showing an indeterminate increase in mRNA in one normal tissue sample and one cancerous tissue sample (see Example 18). However, there is no evidence regarding whether or not PRO1328 mRNA or polypeptide levels are reliably increased or decreased in a cancer. Furthermore, as discussed in the previous Office Action (23 December 2004, page 9), what is often seen is a *lack* of correlation between

expression and increased peptide levels (Pennica, et al, 1998, Proc. Natl. Acad. Sci., 95: 14717-14722). As discussed by Haynes et al (1998, Electrophoresis, 19: 1862-1871), polypeptide levels cannot be accurately predicted from mRNA levels, and that, according to their results, the ratio varies from zero to 50-fold (page 1863). The literature cautions researchers against drawing conclusions based on *small* changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (2003, Journal of Proteome Research 2: 405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). Applicants dispute Hu et al's findings, stating: "Hu et al manipulated various aspects of the input data" (Response, page 12). Applicants also point out that the Hu, et al data "may reflect a bias in the literature" (Response, page 7)." However, it is difficult to fault "bias in the literature" in the Hu article when the study simply aimed to compare message with protein for 2286 genes in breast cancer. And a discussion, by the authors, of the *possible* sources of error in an extensive survey study is not unusual in a well-crafted research paper. Regardless of whether there is a correlation between mRNA and protein levels in a sample, the data presented in the instant Application do not show a consistent positive response since only one measurement was made.

Given the small increase in expression of PRO1328, in one cancer, and the evidence

provided by the current literature, it is clear that one skilled in the art would not assume that a small increase or decrease in expression would correlate with experimentally significant increased or decreased mRNA or polypeptide levels. Further research needs to be done to determine whether the small increase in PRO1328 mRNA in one normal tissue and one cancer tissue supports a role for the antibody in the cancerous tissue; such a role has not been suggested by the instant disclosure. Such further research requirements make it clear that the asserted utility is not yet in currently available form, i.e., it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. As discussed in Brenner v. Manson, (1966, 383 U.S. 519, 148 USPQ 689), the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and,
>
> "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Accordingly, the Specification's assertions that the claimed PRO1328 antibodies have utility in the fields of cancer diagnostics and cancer therapeutics are not substantial.

There is no evidentiary support that PRO1328 is involved in the etiology of cancer in the two tissues disclosed in the instant Application. Furthermore, as noted above, the increase in PRO1328 mRNA in one normal tissue and one cancerous tissue, and then displaying merely a two-fold increase, points away from its role in a disease. At any rate, one negative result

combined with one positive result is too incomplete a study to make a conclusion about PRO1328 and cancer. The *specific* function of the PRO1328 polypeptide has not been disclosed by Applicants or by recent research.

As discussed in the previous Office Action (23 December 2004), a 2-fold increase in message is not large and may be less likely to indicate disease (Hu, et al, 2003, Journal of Proteome Research 2:405-412), or may be sufficient (Applicant's Response, page 12). However, the type or magnitude of increase is not at issue in this case. All that is known about the PRO1328 mRNA is that it is increased in one normal tissue sample and one cancer. It cannot be determined what the function of PRO1328 is in the two tissues; certainly the tissues provide no clues. It is hard to conceive of a specific and substantial utility for a nucleic acid or a peptide encoded by the nucleic acid for which so little consistent data or information is given. For example, what might be the connection between the normal tissue and the cancerous tissue that would provide clues to the mRNA's function?

Because Applicants do not know the function of the PRO1328 polypeptide, *detecting* (by use of the claimed antibodies) the PRO1328 polypeptide has no specific function, since it is not useful to detect a protein for which a function has not yet been identified, and additionally might be expressed in several unrelated normal tissues. Since the asserted utility for the PRO1328 antibody is not in currently available form, the asserted utility is not substantial.

Conclusion

No claims are allowed.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
31 August 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER